REMARKS

The enclosed is responsive to the Examiner's Office Action mailed on April 26, 2010. Claims 28 and 32 have been amended. Claim 30 has been canceled. No claims have been added. Claims 1-22, 24-26, 28, and 29 are withdrawn from consideration. No new matter has been added.

Applicants reserve all rights under the doctrine of equivalents.

Claim Rejections – 35 U.S.C. § 102

Claim 23 stands rejected under 35 U.S.C. § 102(b) as being anticipated by L. Engman et al. Tetrahedron (1994) 50(9), pages 2929-2938, (hereinafter "Engman") or in the alternative being anticipated by H.S. Hsieh et al. Biochemistry (1975) 14(8), pages 1632-1636, (hereinafter "Hsieh").

Engman discloses an investigation of a gluthanione peroxidase-like catalysis of α-(phenylselenenyl) ketones. In particular, Engman discloses reacting S-(phenylselenenyl)glutathione with a further glutathione to form G-S-S-G, where G denotes glutathione residue (see Scheme 3 on page 2931 of Engman). For example, Engman discloses the following reaction:

G-SSe-Ph + GSH → G-SS-G + Ph-SeH

Glutathione is a peptide which contains a cysteine residue, and is not a carbohydrate residue.

Similar to Engman, Hsieh also discloses reacting S-(phenylselenenyl)glutathione with a further glutathione to form G-S-S-G, where G denotes glutathione residue (see Scheme 3 on page 1635 of Hsieh). For example, Hsieh discloses the following reaction:

G-SSe-H + GSH → G-SS-G + H_2Se

Applicants have amended independent claim 23 with the subject matter of now-canceled claim 30. Claim 23, as amended, reads as follows:

> A method of chemically modifying a protein, peptide or amino acid comprising at least one selenenylsulfide group, the method comprising reacting the protein, peptide or amino acid with a carbohydrate compound comprising a thiol group.

(Claim 23, as amended)(emphasis added).

Support for the amendment is found at p. 2, lines 13 – 29 of the specification and thus is no new matter has been added. In claim 23, applicants claim "reacting the protein, peptide or amino acid with a carbohydrate compound comprising a thiol group." The Examiner apparently admits that neither Engman nor Hsieh disclose reacting a protein, peptide, or amino acid with "a carbohydrate compound comprising a thiol group" because the Examiner employs different prior art to reject the subject matter contained in now-canceled claim 30. Furthermore, neither Engman nor Hsieh disclose a reactant that is a carbohydrate containing thiol. Thus, neither Engman nor Hsieh disclose the claim element. Therefore, applicants respectfully submit that neither Engman nor Hsieh anticipate claim 23. Applicants, accordingly, respectfully request the withdrawal of the rejection under 35 U.S.C. § 103.

Claim Rejections – 35 U.S.C. § 103

Claims 23 and 30-32 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over B.G. Davis et al. et al. Tetrahedron: Asymmetry (2000) 11, pages 245-262, (hereinafter "Davis"), Engman, Hsieh, and U.S. Patent/Publication No. 5,759,823 by Wong, (hereinafter, "Wong"). Claim 30 is canceled and the rejection of this claim is moot.

Davis discloses preparing glycomethanethiolsulfonate (glycol-MTS) protein glycosylation reagents. The reagents are used in a controlled site-selective gluycosylation

strategy that combines site-directed mutagenesis with chemical modification. Davis, however, does not disclose reagents that contain selenium.

Wong discloses oligosaccharide compounds that are substrates and inhibitors of glycosyltransferase and glycosidase enzymes.

Claim 23, as amended, reads as follows:

> A method of chemically modifying a protein, peptide or amino acid comprising at least one selenenylsulfide group, the method comprising reacting the protein, peptide or amino acid with a carbohydrate compound comprising a thiol group.

(Claim 23, as amended)(emphasis added).

Applicants respectfully submit that the combination of Davis, Engman, Hsieh, and Wong is improper. The Examiner asserts that combining Davis, Engman, Hsieh, and Wong would be obvious to one of ordinary skill in the art. A summary of the different reactions for each of the relevant art is given as:

Engman: G-SSe-Ph + GSH → G-SS-G + Ph-SeH

Hsieh: G-SSe-H + GSH → G-SS-G + H_2Se

Davis: Carbohydrate-S-SO_2Me + Protein-SH → Protein-S-S-Carbohydrate

Applicants: Carbohydrate-S-Se-R + Protein-SH → Protein-S-S-Carbohydrate + R-SeH.

As is evident from the reactions, the difference between Davis and the claimed invention is that Davis' reactants includes "S-SO_2" group whereas applicants' reactants includes a "selenenylsulfide group" (S-Se group). In order to demonstrate a *prima facie* case of obviousness, the Examiner must demonstrate that it would be obvious to one of ordinary skill in the art to use the method of Davis for the Davis' reactant that has an S-Se group instead of the S-SO_2 group as disclosed by Davis. An Examiner can support an obvious combination if

a simple substitution of one known element for another obtain predictable results (MPEP §2143). The Examiner, however, has failed to demonstrate that substituting Davis' S-SO_2 with the S-Se group in Davis' reactants has the same or similar reactive properties and would lead to the same chemical products. Thus, applicants' respectfully submit that it would not be obvious for one of ordinary skill in the art to simply substitute the S-So_2 group in Davis' reactants is an S-Se group of Engman or Hsieh. Therefore, applicants' respectfully submit that is would not be obvious to combine Engman or Hsieh with Davis.

Instead, the Examiner asserts that one of ordinary skill in the art would be motivated to combine Engman, Hsieh, and Wong with Davis because of the hope of releasing PhSeH as a by-product which could be monitored by spectroscopic means to follow the reaction to completion. The Examiner, however, has not cited references that support the notion that disclose that the Soret band of the benzene-selenolate is red shifted from that of the peptide/protein bound phenylselenyl compound. Secondly, modifying the reaction disclosed in Davis to ensure that it is easier to follow would only make sense if the skilled person would reasonably expect that using Se in place of SO2 is expected to work. As noted above, applicants do not believe that the skilled person would make this assumption.

The Examiner further asserts that one of ordinary skill in the art would have been motivated to modify the reaction disclosed in Davis since the phenylselenyl modified thiol sugars would have been easier to synthesize than the equivalent thiosulfonate analogues disclosed in Davis. In particular, the Examiner has noted that the reagents of the present invention could have been synthesized from commercially available thiol sugars. Even if this is the case, this does not explain the why the skilled person would have expected that using a selenenylsulfide modified thiol sugar in place of a thiosulfonate modified thiol sugar as disclosed in Davis would have yielded a successful reaction.

In addition, Engman and Hsieh are directed to probing the reaction mechanism of selenium-containing glutatione peroxidases but are not concerned with the chemical modification of proteins in general. Therefore, one of ordinary skill in the art would not be motivated to apply the disclosures of Engman and/or Hsieh to provide alternative methods of modifying the proteins as disclosed in Davis.

Thus, applicants respectfully submit that one of ordinary skill in the art would not look to combine Davis with Engman and/or Hsieh. Therefore, suggesting that these references are combinable relies of impermissible hindsight based on the applicants' own disclosure.

Accordingly, claim 23 and claims 31 and 32 that depend on claim 23 are not rendered obvious by Davis, Engman, Hsieh, and Wong.

CONCLUSION

Applicants respectfully submit that in view of the amendments and arguments set forth herein, the applicable objections and rejections have been overcome. Applicants reserve all rights under the doctrine of equivalents.

Pursuant to 37 C.F.R. 1.136(a)(3), applicants hereby request and authorize the U.S. Patent and Trademark Office to (1) treat any concurrent or future reply that requires a petition for extension of time as incorporating a petition for extension of time for the appropriate length of time and (2) charge all required fees, including extension of time fees and fees under 37 C.F.R. 1.16 and 1.17, to Deposit Account No. 02-2666.

Respectfully submitted,

BLAKELY, SOKOLOFF, TAYLOR & ZAFMAN LLP

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Eric S. Replogle
Reg. No. 52,161

1279 Oakmead Parkway
Sunnyvale, CA 94085-4040
(408) 720-8300